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Chemical:	**Pyridate**
PC Code:	**128834**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**11/23/99**
File ID:	**DPD259289**
Accession Number:	**412-01-0084**

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 23-NOV-1999

SUBJECT: **Pyridate - Acute and Chronic Dietary Exposure Analyses.** PP#s: 6F04754 and 9E06025. Chemical#: 128834. DP Barcode: D259289. Case #: 287949. Submission #: S508455.

FROM: Jennifer E. Rowell, Chemist
Registration Action Branch 1
Health Effects Division (7509C)

THROUGH: Michael Doherty, Chemist
Manying Xue, Chemist
Dietary Exposure Science Advisory Council

Melba Morrow, D.V.M., Branch Senior Scientist
Registration Action Branch 1
Health Effects Division (7509C)

TO: George F. Kramer, Ph.D., Chemist
Registration Action Branch 1
Health Effects Division (7509C)

Action Requested

Provide an estimate of the dietary exposure and associated risk for pyridate resulting from existing tolerances and proposed tolerance levels for residues in or on mint at 0.2 ppm(PP# 9E06025), collards at 0.03 ppm (PP# 6F04754), and the Brassica Head and Stem subgroup at 0.03 ppm (PP# 6F04754). The most recent dietary exposure estimate was performed in conjunction with the Section 18 request for use on mint (Memo, J. Rowell 5/10/99; Barcode D255654).

Executive Summary

Acute and chronic (non-cancer) dietary exposure analyses for pyridate were performed using the Dietary Exposure Evaluation Model (DEEM™). For the acute and chronic analyses, published and proposed tolerance level residues were used and 100% crop treated (CT) was assumed for all commodities. Therefore, the acute risk was analyzed at the 95th percentile. The results of the acute and chronic analyses indicate that the acute and chronic dietary risks associated with the existing and proposed uses of pyridate are less than 1% of the Population Adjusted Doses (PADs) for the general U.S. population and all population subgroups, which is well below HED's level of concern.

Toxicological Endpoints

On October 21, 1997, the Health Effects Division's (HED's) Hazard Identification Review Committee (HIARC) met to evaluate the toxicology data base of pyridate with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to pyridate as required by the Food Quality Protection Act (FQPA). In addition, the Committee also re-assessed the doses and endpoints selected for acute dietary, chronic dietary (RfD) as well as occupational and residential exposure risk assessments (Memo, J. Rowland 11/3/97). A summary of the dietary doses and toxicological endpoints chosen by HIARC is listed in Table 1.

Table 1. Summary of Dietary Doses and Toxicological Endpoint Selections for Pyridate.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL= 20 UF = 100	Clinical signs indicative of neurotoxicity characterized as ataxia and emesis were observed within 1-3 hours post-dosing on the first day and persisted for duration of study. LOAEL = 60 mg/kg/day.	90-Day Feeding Study - Dog
		Acute RfD [a] = Acute PAD [b] = 0.20 mg/kg/day	
Chronic Dietary	NOAEL = 10.8 UF = 100	Based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL) in a 2-year feeding study in rats. (This was supported by the parental systemic toxicity NOAEL and LOAEL established in the three-generation reproduction study in rats. In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations)).	Chronic Toxicity/Carcinogenicity Study - Rat
		Chronic RfD [a] = Chronic PAD [b] = 0.11 mg/kg/day	

a $\quad RfD = NOAEL / UF$

b $\quad PAD\ (acute\ or\ chronic) = RfD\ (acute\ or\ chronic) / FQPA\ Safety\ Factor$

FQPA Recommendation

The FQPA Safety Factor Committee met on October 4, 1999 to evaluate the hazard and exposure data for pyridate and recommended that the FQPA Safety Factor (as required by Food Quality Protection Act of August 3, 1996) be removed (i.e. reduced to 1x) in assessing the risk posed by pyridate. This decision is based on 1) the toxicology database is complete for the assessment of the effects following *in utero* and/or postnatal exposure to pyridate; 2) the toxicity data provided no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure; 3) the requirement of a developmental neurotoxicity study is not based on the criteria reflecting some special concern which are generally used for requiring a DNT study and an FQPA safety factor (e.g.: neuropathy in adult animals; CNS malformations following prenatal exposure; brain weight or sexual maturation changes in offspring; and/or functional changes in offspring) and therefore does not warrant an FQPA safety factor; and 4) the exposure assessments will not underestimate the potential dietary and non-dietary exposures for infants and children from the use of pyridate (Memo, B. Tarplee 10/15/99).

The Population Adjusted Dose (PAD) is a modification of the acute or chronic RfD to accommodate the FQPA Safety Factor. The PAD is equal to the acute or chronic RfD divided by the FQPA Safety Factor. **Since the HED FQPA SFC determined to remove the 10x safety factor (i.e. reduce to 1x), the RfD is identical to the PAD.**

Residue Information

Tolerances have been established for the residues of pyridate in or on cabbage at 0.03 ppm; chickpeas, dry at 0.1 ppm; corn, fodder at 0.03 ppm; corn, forage at 0.03 ppm; corn, grain at 0.03 ppm; corn, silage at 0.03 ppm; and peanut, nutmeat at 0.03 ppm [40 CFR §180.462(a)]. Time-limited tolerances in conjunction with a Section 18 registration have been established for peppermint, tops and spearmint, tops at 0.3 ppm (expires 12/31/01) [40 CFR §180.462(b)].

For the acute and chronic analyses, tolerance level residues were used and 100% CT was assumed for all commodities. In addition, DEEM™ default concentration factors were used for all commodities. A summary of the residue information used in the acute and chronic analyses is attached (Attachment 1).

Consumption Information

HED conducts dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM™), which incorporates consumption data generated in USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1989-1992. For chronic dietary risk assessments, the three-day average of consumption for each sub-population is combined with residues in commodities to determine the average exposure in mg/kg/day.

Results/Discussion

Acute Dietary Exposure Analysis

A Tier 1 acute analysis was performed for the general U.S. population and all population subgroups using published and proposed tolerance levels for all commodities. 100% CT information was used for all commodities. For acute dietary risk, HED's level of concern is >100% aPAD. Dietary exposures and associated acute risk for general U.S. population and all population subgroups are shown in Table 2. The other subgroups included in Table 2 are those which represent the highest dietary exposures for their respective subgroups (i.e., children, infants, females, and males). A full listing of dietary exposures is attached (Attachment 2).

Table 2. Summary of Results of Acute DEEM Analysis for Pyridate at 95th Percentile.

	95th Percentile		99th Percentile		99.9th Percentile	
Subgroups	**Exposure (mg/kg/day)**	**% aPAD**	**Exposure (mg/kg/day)**	**% aPAD**	**Exposure (mg/kg/day)**	**% aPAD**
U.S. Population (48 states)	0.000151	<1	0.000269	<1	0.000453	<1
Non-nursing Infants (<1 year)	0.000278	<1	0.000442	<1	0.000682	<1
Children (1-6 years)	0.000303	<1	0.000442	<1	0.000696	<1
Females (13+years/nursing)	0.000149	<1	0.000252	<1	0.000254	<1
Males (13-19 years)	0.000141	<1	0.000216	<1	0.000353	<1

At the 95th percentile, the %aPADs were <1. For acute dietary risk, HED's level of concern is >100% aPAD. The results of the acute analysis indicate that the acute dietary risk associated with the existing and proposed uses of pyridate does not exceed HED's level of concern.

Chronic Dietary Exposure Analysis

The chronic analysis was performed using published and proposed tolerance levels for all commodities. 100% CT information was used for all commodities. For chronic dietary risk, HED's level of concern is 100% cPAD. Dietary exposures for the U.S. population and other subgroups are presented in Table 3. The other subgroups included in Table 3 represent those with the highest dietary exposures for their respective subgroups (i.e., children, infants, females, and males). A full listing of chronic dietary exposures is attached (Attachment 3).

Table 3. Summary of Results from Chronic DEEM Analysis of Pyridate.

Subgroups	**Exposure (mg/kg/day)**	**% cPAD**
U.S. Population (48 states)	0.000048	<1
Non-nursing Infants	0.000121	<1
Children 1-6 yrs	0.000114	<1
Females 13+ (not pregnant/not nursing)	0.000046	<1
Males 13-19 yrs	0.000057	<1

The chronic risks were <1%. For chronic dietary risk, HED's level of concern is >100% cPAD. The results of the chronic analysis indicate that the chronic dietary risk associated with the existing and proposed uses of pyridate does not exceed HED's level of concern.

Attachments

Attachment 1: Pyridate Residue File for Acute and Chronic DEEM™ Analyses.
Attachment 2: Pyridate Acute DEEM™ Analysis (J. Rowell, 11/9/99).
Attachment 3: Pyridate Chronic DEEM™ Analysis (J. Rowell, 11/9/99).

cc (w/attachments): J.Rowell (RAB1); M.Sahafeyen (CEB1); PP#s 6F04754 and 9E06025.
RDI: DE SAC [M. Doherty (11/16/99), M. Xue (11/18/99)]; M.Morrow (11/19/99)
J.Rowell:806W:CM#2:(703)305-5564:7509C:RAB1

Attachment 1: Pyridate Residue File for Acute and Chronic DEEM™ Analyses.

Filename: C:\JRDeem\Pyridate\128834.r96
Chemical name: Pyridate
RfD(Chronic): .11 mg/kg bw/day NOEL(Chronic): 10.8 mg/kg bw/day
RfD(Acute): .2 mg/kg bw/day NOEL(Acute): 20 mg/kg bw/day
Date created/last modified: 11-09-1999/08:42:33/8 Program ver. 6.77
Comment: Pyridate on Mint, Brassica Head and Stem Subgroup, and Collards. Requested by G. Kramer. The 10x FQPA Safety Factor was removed (10/15/99), therefore the PAD and RfD are equivalent.

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
403	O	Peanuts-butter	0.030000	0	1.890	1.000	8F3606
940	O	Peanuts-hulled	0.030000	0	1.000	1.000	8F3606
293	O	Peanuts-oil	0.030000	0	1.000	1.000	8F3606
310	O	Peppermint	0.200000	0	1.000	1.000	Pending, 9E6025
311	O	Peppermint-oil	0.200000	0	1.000	1.000	Pending, 9E6025
312	O	Spearmint	0.200000	0	1.000	1.000	Pending, 9E6025
313	O	Spearmint-oil	0.200000	0	1.000	1.000	Pending, 9E6025
168	5A	Broccoli	0.030000	0	1.000	1.000	Pending, 6F4754
451	5A	Broccoli-chinese	0.030000	0	1.000	1.000	Pending, 6F4754
169	5A	Brussels sprouts	0.030000	0	1.000	1.000	Pending, 6F4754
170	5A	Cabbage-green and red	0.030000	0	1.000	1.000	Pending, 6F4754
383	5B	Cabbage-savoy	0.030000	0	1.000	1.000	Pending, 6F4754
171	5A	Cauliflower	0.030000	0	1.000	1.000	Pending, 6F4754
172	5B	Collards	0.030000	0	1.000	1.000	Pending, 6F4754
175	5A	Kohlrabi	0.030000	0	1.000	1.000	Pending, 6F4754
259	6C	Beans-dry-garbanzo/chick pea	0.100000	0	1.000	1.000	
267	15	Corn grain-bran	0.030000	0	1.000	1.000	8F3606
266	15	Corn grain-endosperm	0.030000	0	1.000	1.000	8F3606
289	15	Corn grain-oil	0.030000	0	1.000	1.000	8F3606
268	15	Corn grain/sugar/hfcs	0.030000	0	1.500	1.000	8F3606
388	15	Corn grain/sugar-molasses	0.030000	0	1.500	1.000	8F3606

Attachment 2: Pyridate Acute DEEM™ Analysis (J. Rowell, 11/9/99).

U.S. Environmental Protection Agency Ver. 6.78

DEEM ACUTE analysis for PYRIDATE (1989-92 data)
Residue file: 128834.r96 Adjustment factor #2 NOT used.
Analysis Date: 11-09-1999/15:52:17 Residue file dated: 11-09-1999/08:42:33/8
Acute Reference Dose (aRfD) = 0.200000 mg/kg body-wt/day
NOEL (Acute) = 20.000000 mg/kg body-wt/day
Run Comment: Pyridate on Mint, Brassica Head and Stem Subgroup, and Collards.
Requested by G. Kramer. The 10x FQPA Safety Factor was removed (10/15/99),
therefore the PAD and RfD are equivalent.

Summary calculations:

	5th Percentile		1st Percentile			0.1st Percentile		
	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
U.S. pop - all seasons:	0.000151	0.08	132766	0.000269	0.13	74355	0.000453	0.23	44135
Hispanics:	0.000153	0.08	130985	0.000270	0.13	74096	0.000444	0.22	45029
Non-hispanic whites:	0.000146	0.07	137276	0.000258	0.13	77544	0.000437	0.22	45716
Non-hispanic blacks:	0.000182	0.09	109823	0.000331	0.17	60461	0.000487	0.24	41079
Non-hispanic other:	0.000146	0.07	137025	0.000297	0.15	67422	0.000588	0.29	34018
All infants (<1 year):	0.000277	0.14	72257	0.000412	0.21	48578	0.000657	0.33	30448
Nursing infants (<1 year):	0.000103	0.05	194037	0.000143	0.07	139685	0.000186	0.09	107401
Non-nursing infants (<1 yr):	0.000278	0.14	71990	0.000442	0.22	45287	0.000682	0.34	29338
Children (1-6 years):	0.000303	0.15	65949	0.000442	0.22	45215	0.000696	0.35	28744
Children (7-12 years):	0.000190	0.10	105201	0.000284	0.14	70440	0.000424	0.21	47190
Females (13+/preg/not nsg):	0.000087	0.04	229793	0.000147	0.07	135741	0.000294	0.15	67915
Females (13+/nursing):	0.000149	0.07	134242	0.000252	0.13	79365	0.000254	0.13	78881
Females (13-19 yrs/np/nn):	0.000116	0.06	172537	0.000173	0.09	115585	0.000312	0.16	64190
Females (20+ years/np/nn):	0.000097	0.05	205574	0.000152	0.08	131512	0.000320	0.16	62448
Females (13-50 years):	0.000104	0.05	193189	0.000160	0.08	124898	0.000303	0.15	65909
Males (13-19 years):	0.000141	0.07	141444	0.000216	0.11	92544	0.000353	0.18	56606
Males (20+ years):	0.000095	0.05	210042	0.000151	0.08	132245	0.000245	0.12	81522
Seniors (55+):	0.000092	0.05	218219	0.000150	0.08	133243	0.000322	0.16	62040

Attachment 3: Pyridate Chronic DEEM™ Analysis (J. Rowell, 11/9/99).

U.S. Environmental Protection Agency Ver. 6.76

DEEM Chronic analysis for PYRIDATE (1989-92 data)

Residue file name: C:\JRDeem\Pyridate\128834.r96 Adjustment factor #2 NOT used.
Analysis Date 11-09-1999/16:20:02 Residue file dated: 11-09-1999/08:42:33/8
Reference dose (RfD, CHRONIC) = .11 mg/kg bw/day
COMMENT 1: Pyridate on Mint, Brassica Head and Stem Subgroup, and Collards. Requested by G. Kramer. The 10x FQPA Safety Factor was removed (10/15/99), therefore the PAD and RfD are equivalent.

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000048	0.0%
U.S. Population (spring season)	0.000047	0.0%
U.S. Population (summer season)	0.000051	0.0%
U.S. Population (autumn season)	0.000049	0.0%
U.S. Population (winter season)	0.000047	0.0%
Northeast region	0.000046	0.0%
Midwest region	0.000049	0.0%
Southern region	0.000050	0.0%
Western region	0.000048	0.0%
Hispanics	0.000048	0.0%
Non-hispanic whites	0.000047	0.0%
Non-hispanic blacks	0.000057	0.1%
Non-hisp/non-white/non-black)	0.000046	0.0%
All infants (< 1 year)	0.000092	0.1%
Nursing infants	0.000023	0.0%
Non-nursing infants	0.000121	0.1%
Children 1-6 yrs	0.000114	0.1%
Children 7-12 yrs	0.000081	0.1%
Females 13-19(not preg or nursing)	0.000046	0.0%
Females 20+ (not preg or nursing)	0.000033	0.0%
Females 13-50 yrs	0.000036	0.0%
Females 13+ (preg/not nursing)	0.000035	0.0%
Females 13+ (nursing)	0.000041	0.0%
Males 13-19 yrs	0.000057	0.1%
Males 20+ yrs	0.000035	0.0%
Seniors 55+	0.000031	0.0%
Pacific Region	0.000047	0.0%